THE ULTIMA TRIAL

Randomized, Controlled Trial of Ultrasound-Assisted Catheter-Directed Thrombolysis for Acute Intermediate-Risk Pulmonary Embolism

Nils Kucher, MD et al. Circulation 2014; 129: 479-486

Patients: Acute PE with RV/LV ratio $\geq 1.0$

Randomization

30 patients

Unfractionated heparin + Ultrasound-assisted CDT using EKOS®

29 patients

Unfractionated heparin

Methods

Unfractionated Heparin†

- IV bolus: 80 IU/kg
- Infusion: 18 IU/kg/hour

Unfractionated heparin administered immediately after randomization

Ultrasound-Assisted Catheter-Directed Thrombolysis Using EKOS®

Insertion of the Catheter System

- In cardiac catheterization lab
- Venous access – common femoral vein;
  - 6F sheath for unilateral PE
  - 10F double-lumen sheath for bilateral PE
- 0.035" guidewire and angiographic catheter to cross occlusion
- With guidewire tip within large lower-lobe segmental branch, angiographic catheter exchanged for EKOS® Drug Delivery Catheter
- Guidewire removed and EKOS® Ultrasound Core Wire inserted
- Infusions started then ultrasound turned on

Infusion Protocol

- rtPA 1mg/h; saline coolant 35ml/h
- Patients monitored in the intermediate or ICU
- After five hours, rtPA reduced to 0.5mg/h
- At 15 (+/- 1) hours, rtPA infusion, saline coolant and ultrasound discontinued
- EkoSonic® devices removed in the intermediate or ICU

† Unfractionated heparin administered immediately after randomization

Indications for use: The EkoSonic® Endovascular System is intended for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature. The EkoSonic® Endovascular System is intended for the infusion of solutions into the pulmonary arteries. The EkoSonic® Endovascular System is indicated for the ultrasound facilitated, controlled and selective infusion of physician-specified fluids, including thrombolytics, into the vasculature for the treatment of pulmonary embolism. Contraindications: This system is contraindicated when, in the medical judgment of the physician, a procedure may compromise the patient’s condition. See device instructions for use for complete prescribing information.
Key Results

Acute PE patients treated with EKOS® showed:

**RV/LV ratio significantly improved at 24 hours**

<table>
<thead>
<tr>
<th></th>
<th>Baseline 24 hrs</th>
<th>Baseline 24 hrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>EKOS® with tPA + Heparin</td>
<td>1.28</td>
<td>0.99</td>
</tr>
<tr>
<td>Heparin</td>
<td>1.20</td>
<td>1.17</td>
</tr>
</tbody>
</table>

**Reduction in RV/LV ratio significantly greater at 24 hours and improved at 90 days**

<table>
<thead>
<tr>
<th></th>
<th>Baseline to 24 hrs</th>
<th>Baseline to 90 days</th>
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<tbody>
<tr>
<td>EKOS® with tPA + Heparin</td>
<td>0.30</td>
<td>0.35</td>
</tr>
<tr>
<td>Heparin</td>
<td>0.24</td>
<td>0.03</td>
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**No deaths or significant bleeding complications**

<table>
<thead>
<tr>
<th>Clinical outcomes at 90 days</th>
<th>EKOS® with tPA + Heparin N = 30</th>
<th>Heparin N = 29</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0</td>
<td>1*</td>
<td>0.49</td>
</tr>
<tr>
<td>Recurrent venous thromboembolism</td>
<td>0</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>0</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>3**</td>
<td>1</td>
<td>0.61</td>
</tr>
</tbody>
</table>

* Rehospitalization and death from advanced pancreatic cancer
** Two patients with transient mild hemoptysis without medical intervention, one patient with groin hematoma requiring manual compression
† One patient with transient anal bleeding following endoscopic removal of colon polyp

**Systolic RV dysfunction significantly improved**

<table>
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<th>Baseline 24hrs 90 days</th>
<th>Baseline 24hrs 90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>EKOS® with tPA + Heparin</td>
<td>100%</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Heparin</td>
<td>P&lt;0.001</td>
<td></td>
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</tbody>
</table>

**CONCLUSION**

ULTIMA confirmed that a fixed-dose, ultrasound-assisted catheter-directed thrombolysis using EKOS® regimen was superior to anticoagulation alone in improving RV dysfunction at 24 hours without an increase in bleeding complications.